

CLAIMS

What is claimed is:

- Feb 7* ✓ 1 An inhibitor of a colony stimulating factor (CSF), which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising an agent which binds to a CSF, an agent which inhibits expression of a CSF, an antagonist of a colony stimulating factor receptor (CSFR), an antibody directed to a CSF or a CSFR, or an agent which inhibits activation of a CSFR, or a pharmaceutically acceptable salt thereof.
- 10 2. The inhibitor of Claim 1 wherein the CSF is a monocyte-colony stimulating factor (M-CSF).
3. The inhibitor of Claim 1 wherein the chemokine is a beta-chemokine.
4. The inhibitor of Claim 1 wherein the CSF is an M-CSF, the chemokine is monocyte chemotactic protein-1 (MCP-1), and the inhibitor is an antibody directed to an M-CSF or an antibody directed to a monocyte-colony stimulating factor receptor (M-CSFR).
- 15 5. The inhibitor of Claim 1 wherein the CSF is an M-CSF, the chemokine is MCP-1, and the inhibitor is an antagonist of an M-CSFR.
6. The inhibitor of Claim 1 wherein the CSF is a granulocyte-colony stimulating factor (G-CSF).
- 20 7. The inhibitor of Claim 1 wherein the chemokine is an alpha-chemokine.
8. The inhibitor of Claim 1 wherein the CSF is a G-CSF, the chemokine is IL-8, and the inhibitor is an antibody directed to a G-CSF or an antibody directed to a granulocyte-colony stimulating factor receptor (G-CSFR).

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9. The inhibitor of Claim 1 wherein the CSF is a G-CSF, the chemokine is IL-8, and the inhibitor is an antagonist of a G-CSFR.
10. The inhibitor of Claim 1 wherein the CSF is a granulocyte macrophage-colony stimulating factor (GM-CSF).
- 5 11. A pharmaceutical composition, comprising an inhibitor of a CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, or excipient.
- 10 12. A method of treating inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising administering to a mammal, in need thereof, a therapeutically effective amount of an inhibitor of a CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, or a pharmaceutically acceptable salt thereof.
- 15 13. The method according to Claim 12 wherein the disease being treated is atherosclerosis.
14. The method according to Claim 12 wherein the disease being treated is sepsis.
- 20 15. The method according to Claim 12 wherein the disease being treated is asthma.
16. The method according to Claim 12 wherein the disease being treated is an autoimmune disease.
- 25 17. The method according to Claim 12 wherein the disease being treated is osteoporosis.

18. The method according to Claim 12 wherein the disease being treated is rheumatoid arthritis.
19. The method according to Claim 12 wherein the disease being treated is osteoarthritis.
- 5 20. A method for screening for an inhibitor of an M-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising analyzing an (M-CSF)-stimulated monocyte population using a Fluorescent Activated Cell Sorter technique.
- 10 21. The method according to Claim 20 wherein the (M-CSF)-stimulated monocyte population is analyzed in whole blood after red blood cell lysis.
22. The method according to Claim 20 wherein the screening method is a high throughput screening method.
- 15 23. The method according to Claim 20 wherein the (M-CSF)-stimulated monocyte population has also been stimulated by MCP-1.
24. The method according to Claim 23 wherein the (M-CSF)-stimulated monocyte population which has also been stimulated by MCP-1, is analyzed in whole blood after red blood cell lysis.
- 20 25. A method for screening for an inhibitor of a G-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising measuring binding of an (I^{125}) G-CSF to a G-CSFR in a (G-CSF)-stimulated neutrophil population.
26. The method according to Claim 25 wherein the screening method is a high throughput screening method.

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27. A method for screening for an inhibitor of a GM-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising measuring binding of an (I^{125}) GM-CSF to a GM-CSFR in a (GM-CSF)-stimulated neutrophil population or analyzing a (GM-CSF)-stimulated monocyte population using a Fluorescent Activated Cell Sorter technique.
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28. A method for screening for an inhibitor of a CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, the method comprising:
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- Step (a) Obtaining CSFR cDNA and corresponding (I^{125})-CSF;
- Step (b) Cloning the CSFR cDNA of Step (a) into a vector;
- Step (c) Stably transfecting the vector of Step (b) into a hematopoietic cell line that resembles circulating leukocytes;
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- Step (d) Quantitating the transfected vector of Step (c) and measuring the binding of said (I^{125})-CSF; and
- Step (e) Screening agents for inhibition of CSF activity using a binding assay comprising the transfected vector of Step (c) and said (I^{125})-CSF.
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29. A method for screening for an inhibitor of an M-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising measuring binding of an (I^{125}) M-CSF to an M-CSFR in an (M-CSF)-stimulated monocyte population.
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30. The method according to Claim 29 wherein the M-CSFR is a soluble M-CSFR.

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